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HYPERTHERMIA IN RHESUS MONKEYS EXPOSED TO A FREQUENCY (225 MHz) NEAR WHOLE-BODY RESONANCE

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PENSACOLA FLORIDA

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SUMMARY PAGE

THE PROBLEM

Microwave energy absorption by man and animals is strongly dependent upon the frequency and orientation of the field with respect to body dimensions. Theoretical and empirical studies have shown that for whole-body exposure, strongest power deposition (resonance) occurs for electric fields polarized along the longest dimension of the body at the frequency such that this long dimension is about 0.4 times the free-space wavelength. This resonant absorption has also been shown to have significance in the biological effects of microwave and radiofrequency (RF) exposure in rodents. This study was conducted to determine the effect on body temperature of whole-body exposure of the rhesus monkey to a near-resonant frequency of RF, and to compare the results to previous work conducted with rhesus monkeys at a frequency much higher than resonance.

FINDINGS

Exposure of rhesus monkeys to 225 MHz radiation caused severe hyperthermia at power densities greater than 5 mW/cm^2 (2.3 W/kg). A comparison of body temperature responses to exposure at two frequencies, 225 and 1290 MHz, indicated that the resonant frequency (225 MHz) is at least two times more effective in causing hyperthermia than the higher frequency, even after considerations of specific absorption rate are included in the analysis. It was concluded, therefore, that the effects on rhesus monkeys of exposure to a resonant frequency (225 MHz) were substantially greater than what could be predicted based upon straightforward comparisons of dosimetric information (SAR) and the effects of exposures to a much higher frequency (1290 MHz).

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INTRODUCTION

As knowledge of the biological effects of radiofrequency (RF) and microwave radiation has developed, greater emphasis has been placed on quantitative documentation of exposure field parameters in studies of biological endpoints. Theoretical and empirical studies have demonstrated that RF absorption by man and animals is strongly dependent upon frequency and orientation of the field with respect to body dimensions. For whole-body exposure, strongest power deposition (resonance) occurs for electric fields polarized along the longest dimension of the body at the frequency such that this long dimension is about 0.4 times the free-space wavelength (4). Specific biological endpoints have been studied in rodents to confirm that this theoretical resonance does in fact have significance in the biological effects of RF exposure. It has been shown that effects on body temperature levels and operant task performance of rats were greater for equivalent exposures to a resonant frequency than to frequencies above or below resonance (2). Schrot and Hawkins (13) found similar relationships in a study of time-to-convulsion in rats and mice exposed to different frequencies. To take into consideration this dependence of RF energy absorption on frequency, the human exposure standard now being considered by the American National Standards Institute (ANSI) establishes lower exposure limits for frequencies in the region of theoretical resonance for whole-body RF absorption by man.

This study was conducted to determine the effect on body temperature of whole-body exposure of the rhesus monkey to a near-resonant frequency of RF, and to compare the results to previous work conducted with rhesus monkeys at a frequency much higher than resonance (6,7). It was observed that comparable body temperature increases were caused by exposure of the monkeys to only about one-eighth the RF field intensity at the resonant frequency (225 MHz) than was required at a much higher frequency (1290 MHz).

PROCEDURES

Juvenile male rhesus monkeys (3.5 to 4.5 kg) were used in these experiments during the period in which they were 27 to 36 months of age. The average crown-rump length of these animals was 46.6 cm. The average crown-sole length when seated in the restraint chair was 69.6 cm. The monkeys were housed individually in standard metal primate cages in a room adjacent to the exposure chamber room. The animals were fed a diet of Wayne Monkey Chow (Allied Mills, Inc., Chicago, IL) supplemented with fresh fruit. Prior to use in an experiment, each monkey was conditioned to restraint in a foamed polystyrene (Styrofoam) restraint chair for up to eight hours at a time.

The microwave exposures were conducted in a commerically available chamber (3.3 x 3.3 x 6.7 m) designed to be virtually anechoic down to 200 MHz (Emerson & Cuming, Inc., Canton, MA, Technical Bulletin #31-2). Continuous wave (CW) microwave power at 225 MHz was provided by a military Type GRT-3 radio set, and was amplified by a cavity-type amplifier (MCL Model 10270). The chair restrained monkey was exposed at a distance of 240 cm from the copper-lined horn antenna. This distance was 0.78 times the normal ($2D^2/\lambda$) far-field spacing. The electric field polarization was vertical, or parallel to the long axis of the animal. Power density measurements were made with a Narda Model 8608 monitor system at the 240 cm position in the absence of both the chair and the animal. These measurements showed a relatively uniform ($\pm 7\%$ from mean) power density over the region occupied by the subject. The mean power densities used in these experiments were 1.2, 2.5, 5.0, 7.5, 10.0, and 15.0 mW/cm^2.

The chamber was ventilated throughout the experiment with air from the surrounding room, with the direction of air flow from back to front with respect to the monkey. Ambient temperature was maintained at 24 ± 2 °C.

In an effort to estimate the amount of energy actually absorbed by a 4 kg rhesus monkey in our exposure system, two simple series of calorimetric determinations were made. In the first series, rectangular boxes of Styrofoam 65 cm high were made of varying widths or depths, from 5 to 15 cm. These boxes were then filled with normal physiological saline (0.9g NaCl/100 ml) held in a plastic bag. Masses between 3 and 9.5 kg were used. These rectangular blocks were irradiated for 10 min at the same location at which monkeys were exposed, and the amount of energy absorbed was calculated from measurements of the rise in temperature of the solution during exposure. In the second series of measurements, a simple model of a rhesus monkey was made by stuffing 4 kg of tissue-equivalent material into a pair of latex surgical gloves. This model had a head, torso, arms, and legs that were similar in dimension to an actual monkey. After determining initial temperature of the model, it was irradiated in a sitting position for 10 min, and the amount of energy absorbed by the phantom was determined in a Thermonetics Model SEC-A-2401 gradient-layer calorimeter by the procedures defined by Olsen and Griner (10).

For exposures of the monkeys, an eight-hour protocol was used. An animal was transferred from his home cage and placed in the Styrofoam restraint chair in the anechoic chamber at 0800. A Vitek Model 101 Electrothermia Monitor was inserted 10 cm into the rectum of the animal to provide continuous body temperature monitoring. The chamber was then closed and rectal temperature was recorded hourly without reentering the chamber until the conclusion of the experiment. Following a two-hour equilibration period, the four-hour microwave exposure was begun at 1000. The criterion was established that if the monkey's rectal temperature exceeded 41.5 °C, the exposure would be terminated. The body temperature was also monitored for two hours (1400-1600) after the exposure period before concluding the experiment. After initial experiments at 7.5 to 15 mW/cm^2, each animal was subjected to this protocol once per week, with exposures of 0 (sham), 1.2, 2.5, or 5.0 mW/cm^2 conducted in random sequence until each animal had been exposed to each level three times. An average of these repeated measures was then calculated to determine the representative value for each animal.

RESULTS

The calorimetric measurements of the rectangular saline models showed a substantial dependence of the SAR on the mass of the model when the height of the model was held constant. These measurements gave SARs that were as much as twice as large for a 3.5 to 4 kg model as for a 7 kg model. The variation in SAR was linear for models between 3 and 7 kg and the relationship was similar when either width or depth was varied to achieve a larger mass. Between 7 and 9.5 kg, the SAR dependence on mass leveled off. The SAR in a 4 kg saline model 65 x 10 x 6.5 cm (H x W x D) was 0.55 (W/kg)/(mW/cm^2). For a 9.5 kg model (65 x 10 x 15 cm), the SAR was 0.26 (W/kg)/(mW/cm^2). The SAR determined calorimetrically in two separate 4 kg tissue-equivalent rhesus monkey models was 0.46 (W/kg)/(mW/cm^2). This value for the tissue-equivalent model was subsequently used as the estimate of the whole-body SAR in the experimental subjects.

The effects on rectal temperature in two rhesus monkeys that were exposed to power densities between 7.5 and 15 mW/cm^2 are illustrated in Figure 1. Repeated experiments were not attempted at these power densities because the monkeys could not adequately dissipate the heat to keep their body temperature below 41.5 °C. The exposure was terminated after only 30 min for one monkey exposed to 15 mW/cm^2, because his rectal temperature reached 42.0 °C. That monkey became very excited after only 10 to 15 min of exposure at this intensity. The monkeys were exposed for 75 or 90 min at 10 or 7.5 mW/cm^2, respectively, before the 41.5 °C criterion was invoked to terminate the exposure.

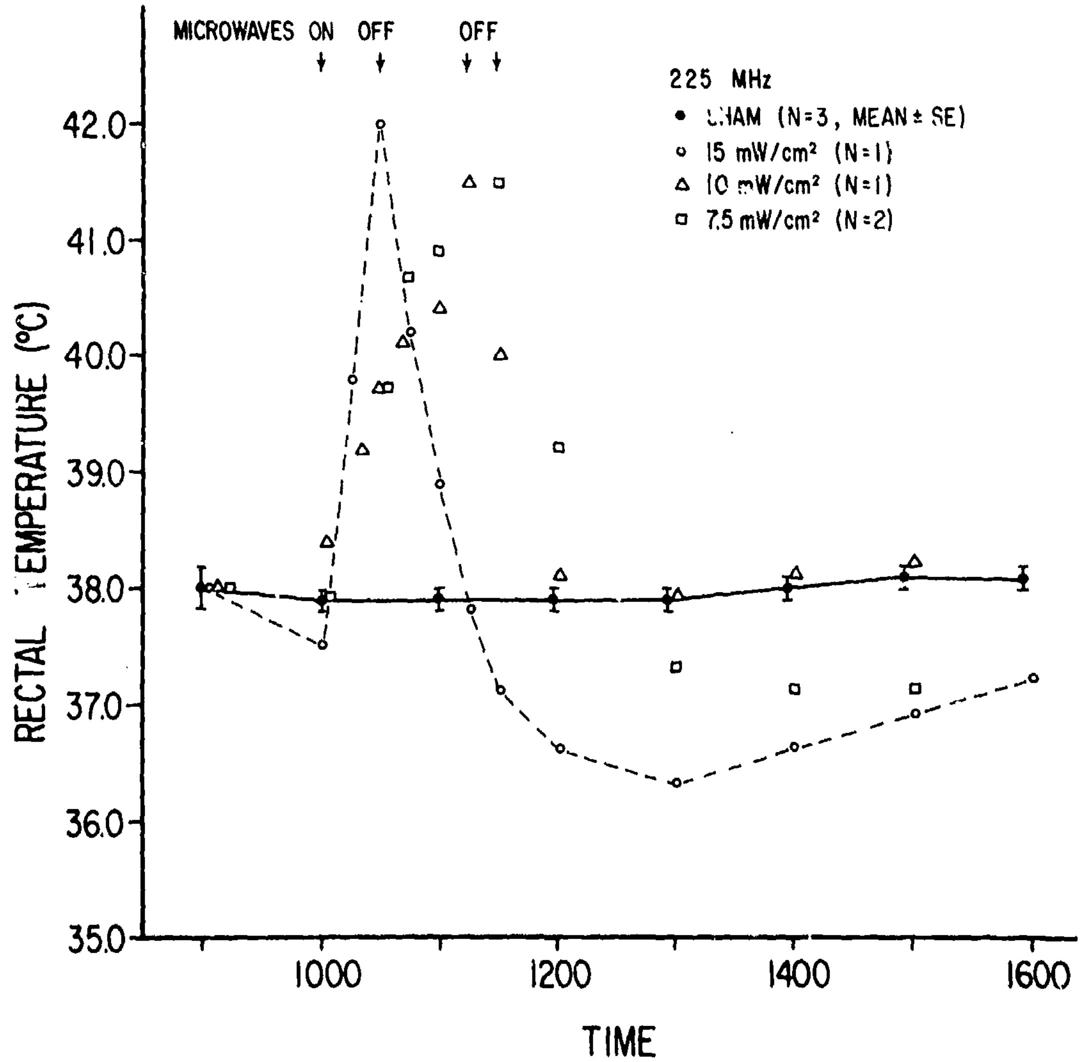

Figure 1: Rectal temperatures of rhesus monkeys sham-exposed or exposed to 225 MHz radiation at power densities of 7.5, 10, and 15 mW/cm^2. The arrows indicate the beginning and end of the exposure.

The mean rectal temperature profiles of monkeys repeatedly exposed to 0, 1.2, 2.5, or 5.0 mW/cm^2 are shown in Figure 2. The mean increase in rectal temperature for the time interval 1100-1400 (hrs 1-4 of the exposure) was 0.1, 0.5, and 1.9 °C above sham level for the three exposure intensities. One of the three monkeys was unable to hold his temperature below 41.5 for the full 4 hr period, so his values are not included in the 1400 h point for 5.0 mW/cm^2. That monkey's inability to maintain a steady-state elevated temperature is also the reason why the error bar at the 1300 h point is considerably larger than at the other points.

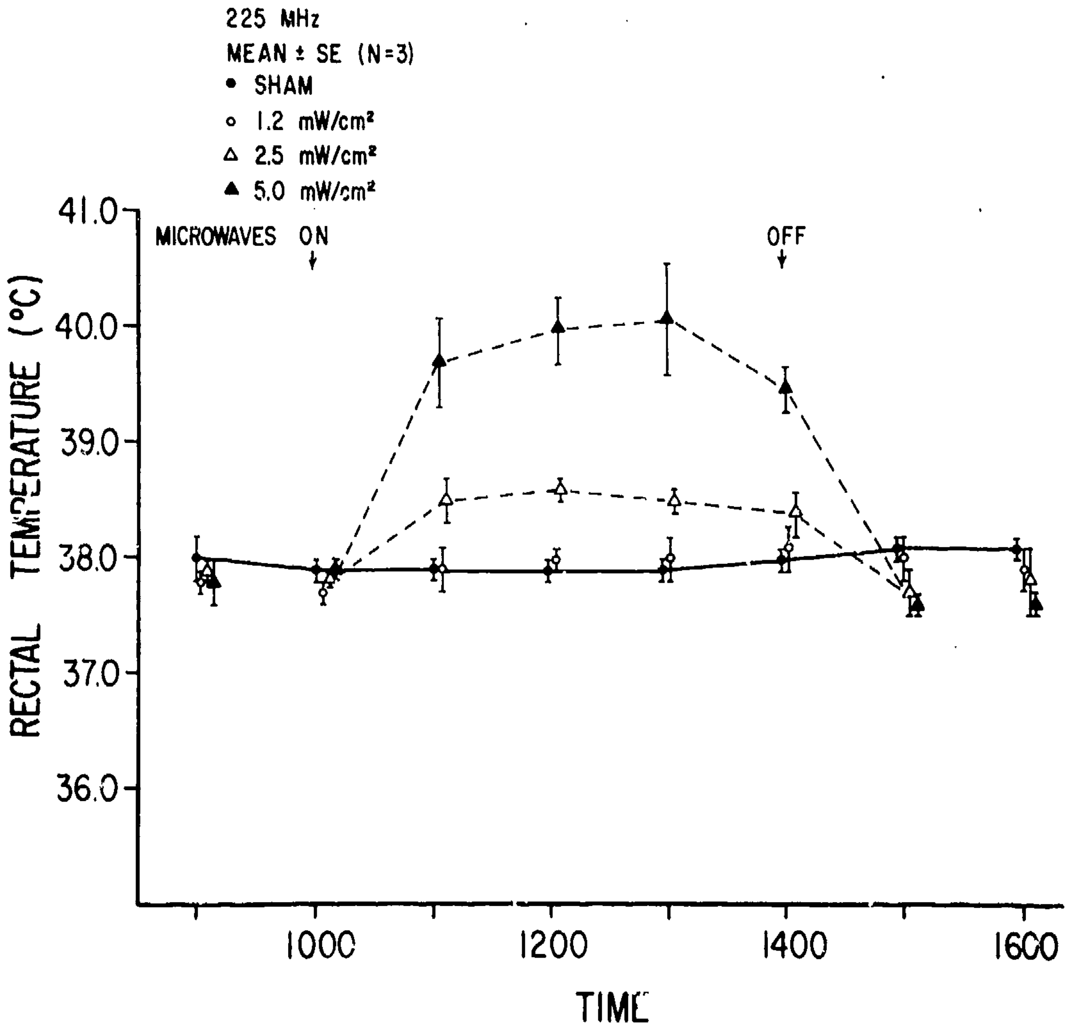

Figure 2: Rectal temperatures of rhesus monkeys sham-exposed or exposed to 225 MHz radiation at power densities of 1.2, 2.5, and 5.0 mW/cm^2. The arrows indicate the beginning and end of the exposure, except for one monkey for which the exposure to 5 mW/cm^2 was prematurely ended (see text).

DISCUSSION

The dramatic increase in rectal temperature of monkeys exposed to intensities between 5 and 10 mW/cm^2 at 225 MHz was quite surprising. If the value for the tissue equivalent rhesus model is taken as representative for this experiment, 0.46 (W/kg)/(mW/cm^2), a 5 mW/cm^2 exposure deposited an average whole-body SAR of 2.3 W/kg in the 4 kg sitting rhesus monkey. The resting metabolic rate (RMR) of this size rhesus monkey is about 2.4 W/kg (1). Thus, an average SAR approximately equal to the RMR represents the maximum exposure level at which these monkeys could maintain a body temperature equilibrium for longer than one hour. At 15 mW/cm^2, with an average SAR of 3 times the RMR, the exposure might have been fatal in less than one hour if it had not been terminated.

The value of average SAR determined in this study with simple models is substantially higher than that determined by other methods (3,10). Using the same exposure facility that was used in these experiments, Olsen and Griner found the average SAR of a tissue-equivalent model of a rhesus monkey weighing 9.5 kg to be 0.285 (W/kg)/(mW/cm^2). According to the Radiofrequency Radiation Dosimetry Handbood 2nd Edition (3), the average SAR of a prolate spheroidal model of a 3.5 kg sitting rhesus monkey at 225 MHz is 0.2 (W/kg)/(mW/cm^2). The dosimetry with simple models reported in this paper was done because the SAR calculated from these other studies seemed so low in relation to the effects on body temperature observed. I believe, based on the demonstrated mass dependence of SAR in the saline block models and the relatively good agreement between the 4 kg saline model and the simple 4 kg tissue-equivalent model that the most representative SAR available for this study is the one for the 4 kg tissue-equivalent model. Additional studies with large rhesus monkeys might indicate whether the effect on body temperature is dependent on the mass of the subject at resonance body length to the same extent as the SAR appears to be. The ratio of sitting height of these monkeys to wavelength at 225 MHz was 0.52.

One of the purposes of this study was to compare the effects of exposure of rhesus monkeys to a frequency near whole-body resonance to the effects on monkeys of exposure to a much higher frequency, 1290 MHz (7). Similar rectal temperature profiles were observed in both experiments, but the power densities used to stimulate those temperature levels were quite different. Because the average SAR is so much greater at 225 MHz than at 1290 MHz, it was expected that a similar biological effect would occur at lower power densities for 225 MHz. However, a comparison of power densities and average SARs used to cause similar increases in body temperature (Table I) reveals that SAR is not sufficient to account for the differences in the effect of these frequencies. Even though average SAR is about 4.5 times greater at 225 than at 1290 MHz, it took a power density roughly 8 to 10 times greater at 1290 MHz to cause the ΔT observed at 225 MHz. The net result was that the average SAR of equivalent effectiveness (for body temperature response) was about one-half as much at 225 as at 1290 MHz. The difference in relative effectiveness of the two frequencies is even more pronounced if the initial rate

TABLE I. Comparison of microwave-induced hyperthermia in rhesus monkeys at 225 MHz and 1290 MHz

	Exposure level to produce a given ΔT[a]	
	0.5-0.6 °C	1.7-1.9 °C
1290 MHz	28 mW/cm^2 (3.0 W/kg)	38 mW/cm^2 (4.1 W/kg)
225 MHz	2.5 mW/cm^2 (1.2 W/kg)	5.0 mW/cm^2 (2.3 W/kg)

[a]ΔT represents the mean difference between the rectal temperature during sham-exposure and the rectal temperature during the period of microwave exposure for which an elevated equilibrium temperature was observed.

of increase in rectal temperature is considered. For the first hour of exposure, mean rectal temperature increased only 0.9 °C for monkeys exposed to 38 mW/cm^2 at 1290 MHz, while it increased 1.8 °C for monkeys exposed to 5 mW/cm^2 at 225 MHz. It should be noted that the monkeys used in the 1290 MHz experiments were considerably larger, with an average mass of about 7.5 kg, than those used in the 225 MHz experiments. The difference in effectiveness may be due to differences in regional SAR within the body. Olsen and his colleagues have shown that at both these frequencies, the greatest regional SAR is in the limbs of the monkey. However, the most significant differences in regional SAR for the two frequencies, 225 and 1290 MHz, are the higher SARs in the deep levels of the torso and at the back surface for 225 MHz exposure (10,11). It may be that the monkey has more trouble dissipating the energy at 225 MHz because he is more uniformly heated, because virtually all surfaces and deep tissues are being heated and there are no body regions that can function as a heat sink. At higher frequencies, the body surface area being heated is less than the total body surface area, allowing the animal a relative advantage in surface area used to dissipate the heat. However, at the resonant frequency, if virtually the entire surface area is being heated, the animal does not have an advantage in surface area available for cooling. This hypothesis has not been tested, but may have heuristic value in the effort to explain the observed differences in the effectiveness of these different frequencies in raising the body temperature of the monkey. It is possible that the rectal temperature is not a reliable indication of deep body temperature at 225 MHz because of high levels of local heating in the colonic area where the probe was positioned. This does not appear to be a valid explanation of the high rectal temperatures observed during 225 MHz exposure because of the cooling rate noted when the radiation was turned off. If the rectal probe location was heated during exposure more than other deep body regions, it should have cooled down more rapidly when the exposure first stopped as blood flow transported that heat to cooler regions of the body. If that were the case, the rate of rectal temperature cooling would decline after a few minutes of internal heat redistribution. That type of cooling process did not occur in these experiments. Instead, rectal temperature decreased at a steady, consistent rate after exposure was terminated, and did not show immediate changes suggestive of substantial local heat redistribution.

The rhesus monkey has been shown to be a good physiological model for man with respect to temperature regulatory mechanisms (5). Thus, these results may be particularly significant in the evaluation of microwave hazards to man. No other reports of exposures of primates to frequencies near whole-body resonance have been published, but the initial results of an independent study using anesthetized rhesus monkeys exposed to 219 MHz were recently reported and were in general agreement with those reported here (In-vivo temperature measurements during whole-body exposure of Macaca species to resonant and non-resonant frequencies, presented at "Microwaves and Thermoregulation: A Symposium," held in New Haven, CT, October 26-27, 19 [illegible], by JH Krupp, USAF School of Aerospace Medicine, Brooks AFB, TX). In their review of the literature on the biological effects data useful for development of RF safety standards for human exposure, Tell and Harlan (14) concluded that it would take between 1.6 and 2.6 times the BMR to raise the deep core body temperature of humans 1 °C. Their conclusion was based on work at frequencies well-above resonance. The results reported here suggested that exposure limits based upon their conclusions may not be adequate for frequencies near whole-body resonance.

One question closely related to the differences in relative effectiveness of exposure to resonant and non-resonant frequencies is the comparison of thermoregulatory responses to microwave exposure and exercise. Exercise-induced hyperthermia appears to be one of the best analogies for microwave-induced hyperthermia, since both situations generate much of the heat in deep tissues (9). In humans, the degree of hyperthermia during exercise is proportional to the relative work load. Humans can sustain exercise at levels of at least 5 times the RMR without experiencing rectal temperatures greater than 1.5 °C above normal (12). Although there is very little data in the literature on exercise-induced hyperthermia in rhesus monkeys, it also appears that rhesus monkeys can exercise vigorously at metabolic rates several times the RMR without causing more than a 1.5 °C rise in rectal temperature (8). However, rectal temperature was increased 1.9 °C in monkeys exposed to 225 MHz when the deposited energy was only equal to the RMR. The obvious question, then, is how can a monkey dissipate heat more effectively when exercising than when that heat is being generated in his tissues passively by exposure to microwave radiation? The answer to that question may involve blood flow in the muscles, which is subject to quite different control stimuli during exercise or microwave exposure. Tell and Harlan (14) also considered the exercise analogy to RF exposure and made the assumption that "the heat stress induced by the absorption of RF energy will not produce higher rectal temperatures than an equivalent metabolic rate caused by exercise." The data on the exposure of rhesus monkeys to 225 MHz indicate that we cannot make such an assumption for RF exposures at a resonant frequency.

In summary, exposure of rhesus monkeys to 225 MHz radiation caused severe hyperthermia at power densities greater than 5 mW/cm^2 (2.3 W/kg). A comparison of body temperature responses to exposure at two frequencies, 225 and 1290 MHz, indicated that the resonant frequency (225 MHz) is at least two times more effective in causing hyperthermia than the higher frequency, even after considerations of SAR are included in the analysis. It was concluded, therefore, that the effects on rhesus monkeys of exposure to a resonant frequency (225 MHz) were substantially greater than what could be predicted based upon straightforward comparisons of dosimetric information (SAR) and the effects of exposures to a much higher frequency (1290 MHz).

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

In order to determine the effect on body temperature of microwave exposure at a frequency near whole-body resonance, juvenile male rhesus monkeys were acutely exposed to 225 MHz whole-body radiation for up to 4 h. The unanesthetized animals were seated in a primate restraint chair and exposed in an anechoic chamber. Rectal temperature was monitored continuously for 2 h before, during, and 2 h after the 4 h exposure period. The monkeys were unable to tolerate exposure to power densities equal to or

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered) greater than 7.5 mW/cm^2 (Specific absorption rate (SAR) of 3.5 W/kg) for longer than 90 min. The criterion for tolerance was that the rectal temperature was not allowed to exceed 41.5 °C. A dose-response series of body temperature curves was obtained for 4 h exposures to 1.2, 2.5, and 5.0 mW/cm^2 for which average increases in temperature were 0.1, 0.5, and 1.9 °C, respectively, when compared to sham-exposure levels. When compared to earlier work with rhesus monkeys exposed to 1290 MHz, these levels of hyperthermia during exposure to 225 MHz occurred at about one-eighth of the power density and about one-half the SAR at which similar effects occurred at 1290 MHz. It was concluded that the effects on rhesus monkeys of exposure to a resonant frequency (225 MHz) were greater than what could be predicted based upon straightforward comparisons of dosimetric information (SAR) and the effects of exposures to a much higher frequency (1290 MHz).